Section I (Amendments to the Claims)

Please amend Claims 100, 101, 103, 111, 113-116, 118-135, cancel Claims 107, 112, 117, and 136, and add new Claims 137-140, as set out in the following listing of the claims of the application.

1 - 99. (Canceled)

100. (Currently Amended) A continuous method of forming particles which comprise microcrystals with a non-hydroscopic inner crystalline core comprising coprecipitant molecules and an outer coating comprising at least one bioactive molecule, comprising the following steps:

(a) providing a continuous stream of an aqueous solution comprising non-polymeric coprecipitant molecules and bioactive molecules, each coprecipitant molecule substantially having a molecular weight of less than 4kDa, wherein the aqueous solution is capable of forming a coprecipitate which comprises the coprecipitant and bioactive molecules with a melting point of above about 90°C;

(b) rapidly admixing the continuous stream of bioactive molecule/coprecipitant molecule solution with a greater volume of a continuous stream of a substantially water miscible organic solvent such that the coprecipitant and bioactive molecules coprecipitate from solution forming ~~said~~ particles which comprise microcrystals with a non-hydroscopic inner crystalline core comprising coprecipitant molecules and an outer coating comprising at least one bioactive molecule, wherein the continuous streams are mixed in a continuous flow process; and

(c) optionally isolating the particles from the organic solvent.

101. (Currently Amended) A method according to claim 100, wherein following mixing with the bioactive molecule the coprecipitant will be at between about 5 and 100 % ~~or between about 20 and 80 %~~ of its aqueous saturation solubility.

102. (Previously Presented) A method according to claim 100, wherein the coprecipitant has a substantially lower solubility in the miscible organic solvent than in the aqueous solution.

103. (Currently Amended) A method according to claim 100, wherein an excess of fully water miscible organic solvent is such that the final water content of the solvent/aqueous solution is generally less than about 30 vol%~~, less than about 10-20 vol% or less than about 8 vol%.~~

104. (Previously Presented) A method according to claim 100, wherein the water miscible organic solvent is selected from any of the following: methanol; ethanol; propan-1-ol; propan-2-ol; acetone, ethyl lactate, tetrahydrofuran, 2-methyl-2,4-pentanediol, 1,5-pentanediol, and various size polyethylene glycol (PEGS) and polyols; or any combination thereof.

105. (Previously Presented) A method according to claim 100, wherein the organic solvent is pre-saturated with the bioactive molecule and/or coprecipitate to ensure that on addition and mixing of the aqueous solution the two components precipitate out together.

106. (Previously Presented) A method according to claim 100, wherein the aqueous phase is added slowly to a large excess of the solvent phase and a mixing process that is turbulent or near turbulent is used.

107. (Cancelled)

108. (Previously Presented) A method according to claim 100, wherein a water miscible organic solvent or mixture of solvents is continuously flowed and mixed with a slower flowing aqueous stream comprising a bioactive molecule and coprecipitant solution producing a combined output flow that contains suspended bioactive molecule coated microcrystal particles.

109. (Previously Presented) A method according to claim 100, wherein upon admixing the bioactive molecule/coprecipitant solution to the excess of the water miscible organic solvent, precipitation of the bioactive and coprecipitant occurs substantially instantaneously.

110. (Previously Presented) Particles as formed according to claim 100.

111. (Currently Amended) Particles obtainable by:

(a) providing an aqueous solution comprising non-polymeric coprecipitant molecules and bioactive molecules, each coprecipitant molecule substantially having a molecular weight of less than 4kDa, wherein the aqueous solution is capable of forming a coprecipitate which comprises the coprecipitant and bioactive molecules with a melting point of above about 90°C;

(b) rapidly admixing the bioactive molecule/coprecipitant molecule solution with a greater volume of a substantially water miscible organic solvent such that the coprecipitant and bioactive molecules coprecipitate from solution forming said particles; and

(c) optionally isolating the particles from the organic solvent.

112. (Cancelled)

113. (Withdrawn but Currently Amended) The A ~~pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the molecules forming the crystalline core have a solubility in water of less than about 150 mg/ml or less than about 80 mg/ml.

114. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the molecules which make up the crystalline core are selected from any of the following: amino acids, zwitterions, peptides, sugars, buffer components, water soluble drugs, organic and inorganic salts, ~~compounds that form strongly hydrogen bonded lattices~~ or derivatives or ~~any~~ combinations thereof.

115. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein bioactive molecules forming a coating on the crystalline core are selected from any molecule capable of producing a therapeutic effect ~~such as an active pharmaceutical ingredient (API)~~.

116. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the coating of bioactive molecules also comprises excipients ~~commonly used in pharmaceutical formulations such as~~ selected from the group consisting of stabilizers, surfactants, isotonicity modifiers and pH/buffering agents.

117. (Cancelled)

118. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the bioactive molecules comprise: anti-inflammatories, anti-cancer agents, anti-psychotic agents, antibacterial agents, anti-fungal agents; natural or unnatural peptides; proteins ~~such as insulin~~, αl-antitrypsin, α-chymotrypsin, albumin, interferons, antibodies; nucleic acids such as

fragments of genes, DNA from natural sources or synthetic oligonucleotides, anti-sense nucleotides, and RNA; and sugars such as any mono-, di- or polysaccharides; and plasmids.

119. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein vaccine coating components include antigenic components of a disease causing agent~~, such as a bacterium or virus, such as diptheria toxoid and/or tetanus toxoid~~.

120. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 120~~ method according to Claim 100, wherein the vaccine components are sub-unit, attenuated or inactivated organism vaccines for a virus selected from the group consisting of ~~such as~~ diphtheria, tetanus, polio, pertussus, ~~and~~ hepatitis A, hepatitis B ~~and~~ hepatitis C, HIV, rabies and influenza.

121. (Withdrawn but Currently Amended) The method of ~~A pharmaceutical formulation according to~~ claim 120, wherein the vaccine is diphtheria taxoid coated D,L-valine or L-glutamine crystals.

122. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the particles are also applicable to administration of polysaccharides linked to proteins, ~~such as HIB (haemopholis influenza B) and~~ pneumococcal vaccines and live virus vaccines~~, such as mumps, measles, rubella~~ and modern flu vaccine ~~components such as MV A vectored influenza vaccine~~.

123. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein vaccine component coated micro-crystals are used for formulation of vaccines developed for cancers~~,~~

~~especially human cancers, including melanomas, skin cancer, lung cancer, breast cancer, colon cancer and other cancers~~.

124. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the particles are selected from the following: a crystalline core of valine and a coating of insulin; a crystalline core of glycine and a coating of antitrypsin, a crystalline core of Na glutamate and a coating of insulin; a crystalline core of methionine and a coating of insulin; a crystalline core of alanine and a coating of insulin; a crystalline core of valine and a coating of insulin; a crystalline core of histidine and a coating of insulin; a crystalline core of glycine and a coating of α-antitrypsin; a crystalline core of glutamine and a coating of albumin: a crystalline core of valine and a coating of oligonucleotides DQA-HEX; a crystalline core of valine and a coating of α1-antitrypsin with a further anti-oxidant outer coating of N-acetyl cystein; a crystalline core of valine and a coating of ovalbumin; a crystalline core of glutamine and a coating of ovalbumin, a crystalline core of valine and a coating of diptheria taxoid; a crystalline core of glutamine and a coating of diphtheria taxoid; a crystalline core of valine and a coating of ~~diptheria~~ tetanus taxoid; a crystalline core of the glutamine and a coating of tetanus taxoid; a crystalline core of the valine and a coating of a mixture of diptheria taxoid and tetanus taxoid; a crystalline core of glutamine and a coating of a mixture of diptheria taxoid and tetanus taxoid.

125. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein following exposure to temperature of up to 60°C for 1 week and reconstitution in aqueous solution the bioactive molecule retains a biological activity substantially similar to that of a freshly prepared formulation.

126. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, wherein the formulation is

delivered to a recipient by parenteral, pulmonary, nasal, sublingual, intravenous, rectal, vaginal, intra-anal or oral administration.

127. (Withdrawn but Currently Amended) The ~~A pharmaceutical formulation according to claim 112~~ method according to Claim 100, comprising a dry powder of bioactive molecule coated microcrystals with a bulk density of less than about 0.3g/ml or less than about 0.1 g/ml.

128. (Withdrawn but Currently Amended) The method of Claim 100, further comprising preparing a ~~A~~ pharmaceutical formulation for pulmonary delivery comprising the particles ~~according to claim 100~~.

129. (Withdrawn but Currently Amended) The method of Claim 128 ~~A pharmaceutical formulation according to claim 129~~, wherein the bioactive molecules ~~suitable for the formation of pulmonary pharmaceutical formulations include any of the following~~ are selected from the group consisting of: therapeutic proteins ~~such as insulin,~~ α1-antitrypsin, interferons; antibodies, ~~and~~ antibody fragments, ~~and~~ antibody derivatives; therapeutic peptide, ~~and~~ hormones; synthetic and natural DNA ~~including DNA based medicines~~; enzymes; vaccine components; antibiotics; pain-killers; water-soluble drugs; water-sensitive drugs; lipids, ~~and~~ surfactants; polysaccharides; ~~or any combination or derivatives~~ and combinations thereof.

130. (Withdrawn but Currently Amended) ~~A pharmaceutical formulation according to claim 129~~ The method of Claim 128, wherein the pulmonary formulation comprising particles are used directly in an inhaler device to provide high emitted doses and high fine particle fractions.

131. (Withdrawn but Currently Amended) ~~A pharmaceutical formulation according to claim 129~~ The method of Claim 128, wherein ~~for pulmonary formulations,~~

the particles have a mass median aerodynamic diameter less than about 10 microns~~, less than about 5 microns or less than about 3.5 microns~~.

132. (Withdrawn but Currently Amended) ~~A pharmaceutical formulation according to claim 129~~ The method of Claim 128, wherein ~~pulmonary formulations are selected to~~ the particles have crystalline cores ~~comprised of amino acids such as~~ comprising one or more of valine, histidine, isoleucine, glycine ~~or~~ and glutamine.

133. (Withdrawn but Currently Amended) ~~A pharmaceutical formulation according to claim 129~~ The method of Claim 128, wherein the ~~pulmonary formulations~~ particles are selected from any of the following: a crystalline core of valine and a coating of ~~a therapeutic protein such as~~ insulin; a crystalline core of histidine and a coating of an enzyme; a crystalline core of valine and a coating of ~~an enzyme inhibitor such as a~~-antitrypsin; a crystalline core of valine and a coating of DNA; a crystalline core of valine and a vaccine coating; ~~and~~ a crystalline core of glutamine and a vaccine coating; and a crystalline core of glutamine and a coating of albumin.

134. (Withdrawn but Currently Amended) The method of Claim 100, wherein the particles are included in a ~~A~~ parenteral formulation ~~comprising particles or suspensions of particles according to claim 100~~.

135. (Withdrawn but Currently Amended) The method of Claim 100, wherein the particles are included in a ~~A~~ sustained or controlled release pharmaceutical formulation ~~(or a depots) comprising particles or suspensions of particles according to claim 100~~.

136. (Cancelled)

137. (New) The method of Claim 100, wherein the bioactive material is selected from the group consisting of peptides, polypeptides, proteins, nucleic acids, sugars, vaccine components, derivatives thereof, and combinations thereof.

138. (New) The method of Claim 100, wherein following mixing with the bioactive molecule the coprecipitant will be at between about 20 and 80 % of its aqueous saturation solubility.

139. (New) The method of Claim 100, wherein an excess of fully water miscible organic solvent is such that the final water content of the solvent/aqueous solution is generally less than about 20 vol%.

140. (New) The method of Claim 122, wherein the protein is Hib, the vaccine is mumps, measles, or rubella, and the modern flu vaccine components are MV A vectored influenza vaccine.